In the Claims[1]

1. (Currently amended) A method to reduce induced apoptosis mediated by a protein-protein interaction between presenilin 2 and a mutated human calcium-binding protein, the method comprising:

administering an effective amount of the mutant calcium-binding protein to inhibit~~ing~~ interaction of presenilin 2 comprising an amino acid sequence as set forth in SEQ ID NO: 1 with the mutated calcium-binding protein, comprising ~~an amino acid sequence set forth in SEQ ID NO: 2~~ a substitution of at least one amino acid residue in the calcium-binding EF-hands of SEQ ID NO: 2, and wherein the calcium-binding EF-hands include amino acid residues at positions 116 to 128 and 161 to 173 of SEQ ID NO: 2.

2. (Original) The method according to claim 1, wherein the presenilin 2 is a human protein.

3. (Currently cancelled)

4. (Original) The method according to claim 3, wherein the calcium-binding protein has reduced interaction with presenilin 1 having an amino acid sequence set forth in SEQ ID NO: 3 relative to the interaction with presenilin 2.

5. (Original) The method according to claim 3, wherein inhibiting the interaction between the presenilin 2 and calcium-binding protein is facilitated by substitution of at least one amino acid residue selected from the group consisting of 287, 288 and 297 of SEQ ID NO: 1.

6. (Original) The method according to claim 5, in which the proline residue at position 287 is substituted by threonine.

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[1] Consistent with the holding of Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., Ltd., et al., 535 U.S. U.S. 722, 152 L.Ed.2d 944 (2002), decided May 28, 2002, any amendments herein that hereafter are deemed to be narrowing amendments by a court of competent jurisdiction in a final unappealed or unappealable decision, are not intended to relinquish any scope of equivalents unforeseeable at the time of this amendment or that relate to aspects of the invention having only a peripheral relation to the basis for the amendment.

7. (Original) The method according to claim 5, in which the alanine residue at position 297 is substituted by threonine.

8. (Currently cancelled)

9. (Currently amended) The method according to claim 1 ~~8~~, wherein at least one acidic residue in the EF-hands is substituted with its amine counterpart, wherein the acidic residue comprises aspartate or glutamate and the respective amine counterpart comprises asparagine or glutamine.

10. (Original) The method according to claim 8, wherein at least one N-terminal residue is substituted at a position 1 to 3 of SEQ ID NO: 2.

11. (Original) The method according to claim 10, wherein an N-terminal glycine is substituted by alanine.

12. (Original) A purified mutant calcium-binding protein comprising an amino acid sequence as set forth in SEQ ID NO: 2 and having a substitution of at least one amino acid residue in at least one calcium-binding EF-hand of SEQ ID NO: 2. (116-128) (161-173)

13. (Original) An isolated nucleic acid molecule encoding a mutant calmyrin protein, the mutant protein comprising at least one amino acid residue substitution at position 2, 127 or 172 of SEQ ID NO: 2.

14. (Original) An expression vector comprising the nucleic acid molecule of claim 13.

15. (Original) A host cell transformed with the expression of vector of claim 14.

16. (Original) The expression vector according to claim 14, wherein the amino acid substitution is selected from the group consisting of G2A, D127N, and E172Q.

17. (Original) A substantially pure mutant calcium-binding protein having an amino acid sequence as set forth in SEQ ID NO: 2 having a substitution of at least one amino acid penultimate N-terminal residue.

18. (Original) An isolated and purified nucleic acid molecule encoding a mutant of human presenilin 2 protein, wherein the mutant comprising at least one amino acid substitution at positions 287, 288 or 297 of SEQ ID NO: 1.

19. (Original) An expression vector comprising the nucleic acid molecule of claim 18.

20. (Original) A host cell transformed with the expression of vector of claim 18.

21. (Original) The host cell according to claim 20, wherein the host cell is a bacterial cell, insect cell, plant cell or animal cell.

22. (Original) The expression vector according to claim 18, wherein the amino acid substitution is selected from the group consisting of P287T, I288L and A298T.

B, 23. (Currently amended) An in vitro ~~A~~ method of reducing apoptosis in neuronal cells comprising: administering a mutated calcium-binding protein in a sufficient amount to effect protein-protein interaction between the mutated calcium-binding protein and ~~with~~ presenilin 2, wherein the mutated calcium-binding protein comprises at least one substitution in the amino acid residues in the calcium-binding EF-hands ~~or in a penultimate N-terminal residue~~ of SEQ ID NO: 2.

24. (Currently amended) An in vitro method to reduce induced apoptosis mediated by protein-protein interaction between presenilin 2 and a calcium-binding protein, the method comprising: administering an effective amount of the mutant calcium-binding protein to inhibit~~ing~~ interaction of presenilin 2 comprising the amino acid sequence as set forth in SEQ ID NO: 1 with calmyrin protein comprising the amino acid sequence as set forth in SEQ ID NO: 2, wherein inhibiting the protein-protein interaction is effected by at least one mutation selected from the group consisting of:

1) substituting at least one amino acid residue at position 287, 288 or 297 of SEQ ID NO: 1;

2) substituting at least one amino acid residue in the calcium-binding EF-hands of SEQ ID NO: 2, wherein the calcium-binding hands include amino acid residues at positions 116 to 128 or 161 to 173 of SEQ ID NO: 2;

3) substituting at least one N-terminal residue at positions 2 or 3 of SEQ ID NO: 2; and

4) substituting at least one amino acid residue at position 2, 127 or 172 of SEQ ID NO: 2.

25. (New) An in vitro method to reduce induced apoptosis mediated by a protein-protein interaction between presenilin 2 and a mutated human calcium-binding protein, the method comprising:

contacting cells with an effective amount of the mutant calcium-binding protein to inhibit interaction of presenilin 2 comprising an amino acid sequence as set forth in SEQ ID NO: 1 with the mutated calcium-binding protein, comprising a substitution of at least one amino acid residue in the calcium-binding EF-hands of SEQ ID NO: 2, and wherein the calcium-binding hands includes amino acid residues at positions 116 to 128 and 161 to 173 of SEQ ID NO: 2.

26. (New) An in vitro method to determine the effectiveness of a test compound to reduce apoptosis mediated by a protein-protein interaction between a calcium-binding protein comprising amino acid residues of SEQ ID NO: 2 and presenilin 2, the method comprising:

administering the calcium-binding protein to cultured cells;

contacting the cultured cells with the test compound; and

determining level of apoptosis in the cultured cells.

27. (New) The purified mutant calcium-binding protein according to claim 12, wherein the substitution of at least one amino acid residue in at least one calcium-binding EF-hand of SEQ ID NO: 2 comprises amino acid residues at positions 116 to 128.

28. (New) The purified mutant calcium-binding protein according to claim 27, wherein the substitution of at least one amino acid residue in at least one calcium-binding EF-hand of SEQ ID NO: 2 comprises amino acid residue at position 127.

29. (New) The purified mutant calcium-binding protein according to claim 28, further comprising a substitutions at amino acid residues 2 and 172.

30. (New) An expression vector comprising a nucleic acid encoding for the mutant calcium-binding protein according to claim 27.

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31. (New) An expression vector comprising nucleic acid encoding for the mutant calcium-binding protein according to claim 28.

32. (New) A purified antibody that binds to a calcium-binding protein comprising an amino acid sequence of SEQ ID NO: 2